

REMARKS

Applicants appreciate the thorough examination of the present application as evidenced by the Office Action dated December 29, 2005 (hereinafter, "Office Action"). Claims 1-3 and 5-13 are pending in the present application upon entry of this Amendment. Applicants have amended Claims 1-3, 6, 7 and 9-13 as further discussed below. Support for these claim amendments can be found in the specification, claims and drawings as originally filed.

Applicants respectfully request entry of this Amendment and allowance of the present application for at least the reasons set forth below. Should there be any issues preventing the allowance of the application upon the Examiner's consideration of the present Amendment, Applicants respectfully request that the Examiner contact the Applicants' representative noted below in order to discuss the outstanding issues.

I. Objections.

The Office Action indicates that the present application fails to comply with the requirements of 37 C.F.R. §1.821 through 1.825. *See* Office Action, page 2. In response, Applicants submit herewith a paper and computer readable copy of a sequence listing submitted in accordance with 37 C.F.R. §1.821 through 1.825.

The Office Action further indicates that the specification is objected to for lack of a catalog number and the full address of the firm from which the pLAT8 plasmid was purchased. *See* Office Action, page 2. The pLAT8 plasmid was obtained from DSM, NV headquartered at Het Overloon 1, 6411 TE Heerlen, The Netherlands, as stated in the present application on page 4, second full paragraph. One desiring to practice the invention may contact DSM in view of the contact information provided in the specification. Alternatively, one may utilize an appropriate expression system that allows the insertion of at least one heterologous coding sequence into the chromosome of the construct and the expression thereof.

Lastly, the Office Action objects to the word "media" a recited in Claim 1. *See* Office Action, page 3. Applicants have amended Claims 1-3 to recite "medium" as suggested by the Examiner.

At least in view of the foregoing, Applicants respectfully submit that the objections to the specification have been addressed, and Applicants respectfully request that the objections to the specification be withdrawn.

II. Claim Rejections Under 35 U.S.C. §112, Second Paragraph.

Claims 1-13 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. *See Office Action, page 3.*

The Office Action states that "Claim 1 is confusing in reciting 'kerA coding segment.'" Office Action, page 3. Applicants have amended Claims 1, 6, 7, 9, 10, 12 and 13 to recite a "kerA coding sequence." This recitation clarifies that the "segment" inserted into the chromosome of the recombinant *Bacillus* is a sequence that encodes keratinase. Accordingly, a one skilled in the art would understand that the coding sequence may or may not include regulatory sequences.

The Office Action further states that "claim 2 is confusing in recitation of the word 'substrate.'" Office Action, page 4. Applicants respectfully submit that one skilled in the art would understand that "substrate" as recited in Claim 2 refers to a protein source upon which an enzyme may interact.

On page 4, the Office Action further states that "Claim 3 is unclear in recitation of the term 'feather meal'. Furthermore, the term 'soy' as used in the claim is unclear, because it refers to the plant as a whole." Applicants respectfully submit that the terms "feather meal" and "soy," as used in the present application, are well understood by those skilled in animal science, and in particular, poultry science. As understood by those skilled in such arts, "feather meal" refers to hydrolyzed poultry feathers, and "soy" is understood by those skilled in the art to encompass soybeans, soybean meal and the hulls. *See attached documents.* Thus, Applicants submit that these terms are clearly understood by those skilled in the art.

The Office Action also states that "Claim 11 is indefinite as reciting an indefinite phrase 'a protease-deficient *Bacillus*.'" Applicants have amended Claim 11 to recite "a keratinase-deficient *Bacillus*."

At least in view of the foregoing, Applicants respectfully submit that the rejections to the specification under 35 U.S.C. §112, second paragraph, have been addressed, and Applicants respectfully request that the objections to the specification be withdrawn.

III. Claim Rejections Under 35 U.S.C. §112, First Paragraph, Written Description.

Claims 1-13 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. *See* Office Action, page 4. More specifically, the Office Action states the following:

The claims are directed to a large and variable genus of methods of using of integrants of *Bacillus* species having at least one heterologous kerA gene inserted into their chromosome. The claims are directed to the use of a large genus of transformants comprising one or several copies of any heterologous kerA gene. Applicants however disclose only Bacillus subtilis species having integrated to its chromosome the *kerA* gene of *Bacillus licheniformis* Disclosing this one recombinant *Bacillus* species transformed with only one identified *kerA* gene does not provide sufficient identifying characteristics of the genus of *Bacillus* species having one or multiple copies of any *kerA* gene integrated into their chromosome.

Office Action, page 5 (citations omitted).

Applicants have amended Claim 1 to recite that the recombinant *Bacillus* is one "selected from the group consisting of *Bacillus licheniformis* and *Bacillus subtilis* and having at least one heterologous *kerA* gene inserted into the chromosome thereof." Applicants respectfully submit that one skilled in the art would appreciate that Applicants were in possession of a recombinant *Bacillus* as recited in amended Claim 1.

The Office Action further indicates that Claim 6 is rejected because "Applicants fail to teach *kerA* gene of *Bacillus subtilis*. This is a complete lack of written description." Office Action, page 5. Applicants specifically state in the specification that "the *kerA* coding segment may be a *Bacillus licheniformis* or *Bacillus subtilis kerA* coding segment." Present Application, page 2, third full paragraph (emphasis added). Moreover, the specification states that "the *kerA* gene has been cloned and expressed from *B. subtilis*." Present Application, page 3, seventh full paragraph. Accordingly, Applicants respectfully submit that the specification teaches that the *kerA* coding segment may be a *Bacillus subtilis kerA* coding segment.

Claim 11 stands rejected on the basis that Claim 11 "imposes limitation on the genus of hosts to be used by the method to only those that are protease-deficient *Bacilli*." Office Action, page 5. As noted above, Applicants have amended Claim 11 to recite "a keratinase-deficient *Bacillus*."

Accordingly, at least in view of the foregoing, Applicants respectfully submit that the claim rejections under 35 U.S.C. §112, first paragraph, as lacking written description, have been addressed, and Applicants respectfully request withdrawal of this rejection.

IV. Claim Rejections Under 35 U.S.C. §112, First Paragraph, Enablement.

Claims 1-13 stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement. *See* Office Action, page 6. More specifically, the Office Action summarizes the enablement rejection by stating, "without a guidance regarding the structure/origin of *kerA* gene, and the name/structure of *Bacillus* protease to be deficient in the host cells the experimentation left to the skilled artisan is improperly extensive and undue." Office Action, page 8.

As noted above, Applicants have amended Claim 1 to recite that the recombinant *Bacillus* is one "selected from the group consisting of *Bacillus licheniformis* and *Bacillus subtilis* and having at least one heterologous *kerA* gene inserted into the chromosome thereof," and Claim 11 has been amended to recite "a keratinase-deficient *Bacillus*." Applicants acknowledge that the touchstone for enablement is whether one reasonably skilled in the art could make and use the invention from the disclosures in the patent application coupled with information known in the art without undue experimentation. *See* Manual of Patent Examining Procedure §2164.01 (citing *In re Wands*, 858 F.2d 731, 737). Applicants respectfully submit that one of ordinary skill in the art could make and/or use the recombinant *Bacillus* according to the methods recited in the amended claims without undue experimentation.

Accordingly, at least in view of the foregoing, Applicants respectfully submit that the claim rejections under 35 U.S.C. §112, first paragraph, as lacking enablement, have been addressed, and Applicants respectfully request withdrawal of this rejection.

V. Claim Rejections Under 35 U.S.C. §103.

Claims 1, 4, 6, 7, 9 and 10 stand rejected under 35 U.S.C. §103 as being obvious over Lin et al. Nucleotide Sequence and Expression of *kerA*, the Gene Encoding a Keratinolytic Protease of *Bacillus licheniformis* PWD-1, Applied and Environmental Microbiology 61: 1469-1474 (1995) (hereinafter, "Lin et al.") in view of van der Laan et al. Cloning, Characterization and Multiple Chromosomal Integration of a *Bacillus* Alkaline Protease

Gene, Applied and Environmental Microbiology 57: 901-909 (1991) (hereinafter, "van der Laan et al."). *See* Office Action, page 8. The Office Action specifically states the following:

It would have been obvious for one having ordinary skills in the art to have *kerA* gene of Lin et al. and express it by integration to a chromosome of *B. subtilis* as van der Laan et al. did, using a commercially available integration plasmid pLAT8. The motivation would be to obtain a cell stably engineered to produce large quantities of keratinase. The motivation is taught by Lin et al., who point out that keratinase is an enzyme degrading feather from poultry waste. Thus, the enzyme is of importance for industrial and environmental reasons. The expectation of success is high, because van der Laan proved the successful production of serine protease by integrants of *Bacillus*.

Office Action, pages 9-10.

In order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, the cited reference or combination of references must teach or suggest all the claim recitations. *See In re Wilson*, 165 U.S.P.Q. 494 (C.C.P.A. 1970) (emphasis added). Second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings in order to arrive at the claimed invention. *See In re Oetiker*, 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992); *In re Fine*, 837 F.2d at 1074; *In re Skinner*, 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Int. 1986). Third, there must be a reasonable expectation of success. *See* M.P.E.P. § 2143. Moreover, the law is clear with respect to obviousness. It is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to "[use] that which the inventor taught against its teacher." *W.L. Gore v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983).

Applicants respectfully submit that the combination of the cited references fails to teach or suggest all the recitations of the pending claims. As noted in the Office Action, "Lin et al. do not teach the production of said keratinase in integrants of *Bacillus*." Office Action, page 9. van der Laan et al. does not supply the missing recitations as this reference is directed to the cloning, characterization and multiple chromosomal integration of a *Bacillus alkaline protease gene*. Accordingly, the combination of the cited references fails to teach or suggest a method of making a keratinase including culturing a recombinant *Bacillus* selected from the group consisting of *Bacillus licheniformis* and *Bacillus subtilis* and having

at least one heterologous *kerA* coding sequence inserted into the chromosome thereof. Furthermore, the combination of the cited references also fails to teach or suggest a method of making a keratinase wherein the recombinant *Bacillus* produces **greater** quantities of keratinase than a corresponding wild-type *Bacillus* that does not have said at least one heterologous *kerA* coding sequence inserted into the genome thereof. Both Lin et al. and van der Laan, to the extent either of these reference discuss keratinase, are **silent** with respect to the **quantity** of keratinase produced. Thus, the cited references fail to teach or suggest all the recitations of the pending claims.

Applicants further submit that the requisite motivation to combine the cited references is lacking. The Office Action states that the "motivation" is taught by Lin et al. noting that keratinase is an enzyme that degrades feather from poultry waste, and thus, the enzyme is important for industrial and environmental reasons. *See* Office Action, page 10. Applicants respectfully submit, however, that the motivation to combine these references is clearly derived from the Applicants' specification. In fact, the Office Action refers to the Applicants' specification and states that "they [Applicants] used a modified protoplast method of Laan et al. for the integration of *kerA* gene into *Bacillus*. Office Action, page 9.

Thus, it is **only** through impermissible hindsight combined with picking and choosing portions of the cited references to the **exclusion** of deficient teachings, as discussed above, is one of ordinary skill in the art able to arrive at the present invention recited in Claim 1. For at least these reasons, Applicants respectfully submit that Claim 1 is not obvious in view of the combination of Lin et al. and van der Laan et al., and Claims 4, 6, 7 and 9-13, which are dependent therefrom, are also non-obvious in view of the cited references.

Accordingly, at least in view of the foregoing, Applicants respectfully submit that the claim rejections under 35 U.S.C. §103 have been addressed, and Applicants respectfully request withdrawal of this rejection.

Attorney Docket No. 5051-653
In re: Jason C. H. Shih et al.
Application No.: 10/661,172
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Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request that all outstanding objections and rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course. The Examiner is invited and encouraged to contact the undersigned directly if such contact will expedite the prosecution of the pending claims to issue. In any event, any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on March 29, 2006.

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